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TECH CENTER 1600/2900

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Pergolizzi et al.

Serial No.: 08/479,995

Filed: June 7, 1995

For: ANALYTE DETECTION UTILIZING
POLYNUCLEOTIDE SEQUENCES,
COMPOSITION, PROCESS AND KIT
(As Previously Amended)

Group Art Unit: 1631

Ex'r: Ardin H. Marschel, Ph.D.

527 Madison Avenue (9th Floor)
New York, NY 10022-4304
December 20, 2002

FILED BY HAND

Commissioner of Patents and Trademarks
Washington, D.C. 20231

COMMUNICATION

TO INTRODUCE REQUEST FOR AN INTERFERENCE UNDER 37 C.F.R. §1.607
(FOLLOWING MARCH 19, 2002, MARCH 26, 2001 AND MARCH 14, 2000 PTO
COMMUNICATIONS)

Dear Sirs:

This Communication follows the March 19, 2002, March 26, 2001 and March 14, 2000 Communications that were issued by the Patent and Trademark Office in connection with the above-identified application. No extension request or fee is believed to be necessary because these three PTO Communications suspended *ex parte* prosecution and there are no outstanding actions to which Applicants must now respond.

Enz-11(C2)(D1)(C2)



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TECH CENTER 1600/2900

Applicants: Pergolizzi, et al.

Group Art Unit: 1631

Application No.: 08/479,995

Examiner: Ardin H. Marschel

Filed: June 7, 1995

Att'y Dkt. No.: ENZ-11(C2)(D1)(C2)

Title: ANALYTE DETECTION UTILIZING POLYNUCLEOTIDE
SEQUENCES, COMPOSITION, PROCESS AND KIT

REQUEST FOR AN INTERFERENCE PURSUANT TO 37 C.F.R. § 1.607

Director of Patents and Trademarks

Washington, D.C. 20231

Sir:

Over five years ago Applicants informed the Examiner that certain patents appear to interfere with the above-captioned Application ("the Pergolizzi Application").¹ Applicants did not file a formal request for an interference but, on March 14, 2000, the Examiner suspended prosecution of the Pergolizzi Application in light of the "potential interference."² Prosecution has remained suspended although no interference has yet been declared. Applicants now respectfully request prompt declaration of an interference between (1) the claims of the Pergolizzi Application and (2) certain claims of U.S. Patent Nos. 4,716,106; 4,882,269; 5,424,188; and 5,124,246.

Immediately below is an Executive Summary of the Invention. Below the Executive Summary is the information required by 37 C.F.R. § 1.607(a), under headings that correspond to its subsections.

¹ On pages 29-31 and 80-84 of the Amendment of July 25, 1997, Applicants reproduced and discussed claims from U.S. Patent Nos. 4,716,106, 4,868,105, and 4,882,269, which were attached to the Amendment as exhibits. An interference with these three patents was also discussed at the Interview of October 29, 1998. See Interview Summary of October 29, 1998.

² Prosecution was suspended pursuant to the Office Communications of March 14, 2000, April 12, 2000, March 26, 2001, and March 19, 2002.

EXECUTIVE SUMMARY OF THE INVENTION

The present invention enhances and streamlines the detection of minute substances in biological or non-biological samples. More specifically, the invention provides a more sensitive, efficient, and universal means for detecting analytes with nucleic acid and immuno assays. *See, e.g.*, Pergollizi Application (p. 7).

In both the invention and the prior art, nucleic acid and immuno assays entail two fundamental events: recognition of the analyte and signaling of that recognition. *Id.* at 1-2. For nucleic acid assays, recognizing the analyte means a nucleic acid sequence, usually called a “probe,” non-covalently binds to a complementary nucleic acid sequence of the analyte. *Id.* For immuno assays, recognizing the analyte means a ligand or receptor binds to a complementary receptor or ligand of the analyte. *Id.*

Signaling is often divided between radioactive signaling, which relies on radioisotopes such as ^{32}P , and non-radioactive signaling, which relies on techniques such as fluorescence or avidin-biotin linkage. *Id.* at 2-3, 19-21. In the prior art, signaling typically employs radioisotopes, which are dangerous, difficult to handle, and whose short half-lives necessitate continuous production of new probes.

In both the invention and the prior art, the recognition event must be coupled with the signaling event. *Id.* at 2-3. However, the prior art means of coupling diverges from that of the invention. In the prior art, the recognition probe and the signal probe both bind to the analyte. *Id.* at 3-4. Either they bind sequentially or, when the recognition and signal probe are one and the same, they bind simultaneously. For example, in generic nucleic acid assays that employ “labeled detection probes,” the recognition and signal probe are one and the same. Thus, the recognition event (detection) is inherently coupled to the signaling event because the labeled detection probes both recognize the analyte and signal that recognition. Yet, generic nucleic acid assays have various disadvantages. Labeling a polynucleotide chain chemically is problematic because it is difficult to selectively label individual nucleotide residues in the chain. *Id.* at 5. Chemical-based procedures require reaction conditions that are generally too vigorous to limit modification to just one or a few nucleotide residues. Dicarbonyl reagents, for example, react indiscriminately with guanine residues, thereby impairing the chain’s ability to recognize (bind to) the analyte. *Id.* at 5. To overcome this, researchers must first synthesize individual modified nucleotides, which often involves elaborate procedures, and then they must incorporate the modified nucleotides into the chain using enzymatic

techniques. *Id.* at 5-6, 24-25. Although enzymatic incorporation diminishes the conflict between a probe's signaling function and its recognition function, it does not erase the conflict, particularly if the researcher desires amplification via a high ratio of signal groups to recognition groups. *Id.* at 4, 6, 22.

In another type of prior art assay, "classic sandwich hybridization," a capture probe binds to one side of the analyte (recognition event) and a separate signal probe binds to the other side of the analyte (signaling event or a precursor thereof), thereby coupling the recognition and signaling events as the analyte is sandwiched between the two probes. A disadvantage of sandwich hybridization is that each unique analyte requires independent synthesis of not only a unique recognition probe but also a unique signal probe—both of which must be complementary to adjacent non-overlapping sections of the specific analyte in question. And again, synthesizing a signal probe efficiently conflicts with that probe's specificity for the analyte.

The invention overcomes these disadvantages by making the signaling probe bind to the recognition probe rather than to the analyte and by including at least two distinct portions on the recognition probe—a first portion that binds to the analyte and a second portion to which the signal probes bind. *Id.* at 7-9. These features obviate the conflict between efficient synthesis of signal probes and their specificity for the analyte. These features also dramatically reduce the need to synthesize unique signal probes—because the same signal probes can be used for any assay. In other words, since the second portion of the recognition probe can always remain the same, the complementary sequence of the signal probe can always remain the same. *Id.* at 8-9, 24-25.

The above-captioned Application, which discloses and claims the generic invention, is entitled to a priority filing date of May 5, 1983, and it has no continuation-in-part in its ancestral line. The interfering patents discussed below, all of which assert priority to 1984, 1985 or 1987, contain claims that define patentably indistinct species of the generic invention.

REQUIREMENTS OF 37 C.F.R. § 1.607(a)

(1) Identification of Patents that Interfere with Application (37 C.F.R. § 1.607(a)(1))

A. U.S. Patent No. 4,716,106

The '106 Patent issued on December 29, 1987, to David J. Chiswell for "Detecting Polynucleotide Sequences." It issued from Application No. 706,747, filed February 28, 1985, which claims the benefit of a British application filed March 1, 1984. Amersham International is the

assignee named on the face of the '106 Patent. Applicants first informed the Examiner that the '106 Patent interferes with the Pergolizzi Application in Applicants' Amendment of July 25, 1997.

B. U.S. Patent No. 4,882,269

The '269 Patent issued on November 21, 1989, to Robert J. Schneider and Thomas E. Shenk for an "Amplified Hybridization Assay." It issued from Application No. 06/940,712, filed December 11, 1986, which is a continuation-in-part of Application No. 06/808,695, filed December 13, 1985. Princeton University is the assignee named on the face of the '269 Patent. Applicants first informed the Examiner that the '269 Patent interferes with the Pergolizzi Application in Applicants' Amendment of July 25, 1997.

C. U.S. Patent No. 5,424,188

The '188 Patent issued on June 13, 1995, to Robert J. Schneider and Thomas E. Shenk for an "Amplified Hybridization Assay." It issued from Application No. 07/963,923, filed October 20, 1992, which is a continuation of Application No. 07/400,831, filed August 29, 1989, which is a divisional of Application No. 06/940,712 (the '269 Patent), filed December 11, 1986, which is a continuation-in-part of Application No. 06/808,695, filed December 13, 1985. Princeton University is the assignee named on the face of the '188 Patent. The '188 Patent is terminally disclaimed over the '269 Patent.

D. US Patent No. 5,124,246

The '246 Patent issued on June 23, 1992, to Michael S. Urdea, Brian Warner, and Thomas Horn for "Nucleic Acid Multimers and Amplified Nucleic Acid Hybridization Assays Using Same." The '246 Patent issued from Application No. 340,031, filed April 18, 1989, which is a continuation-in-part of Application No. 252,638, filed September 30, 1988, which is a continuation-in-part of Application No. 185,201, filed April 22, 1988, which is a continuation-in-part of Application No. 109,282, filed October 15, 1987. Chiron Corporation is the assignee named on the face of the '246 Patent. Applicants first apprised the Examiner of the existence of the '246 Patent in Applicants' Amendment of March 5, 1996. See also Amendment of July 25, 1997 (p.57).

(2) Presentation of Proposed Count (37 C.F.R. § 1.607(a)(2))

Proposed Count 1 is set forth below and in Appendix A.

A hybridization or immuno assay for detecting an analyte, comprising:

(A) providing one or more bridge entities, wherein each bridge entity comprises one or more first portions and one or more second portions, wherein each first portion is capable of binding non-covalently to the analyte, and wherein each second portion is capable of binding non-covalently to one or more signal probes and is substantially incapable of binding to the analyte;

(B) providing said one or more signal probes, wherein each signal probe is capable of binding non-covalently to at least one segment of the one or more second portions and is substantially incapable of binding to the analyte;

(C) detecting the analyte by detecting one or more radioactive or nonradioactive signal moieties provided or afforded by the one or more signal probes; and

(D) wherein optionally: (i) the analyte, bridge entities or signal probes are immobilized, or (ii) step (B) is performed before step (A).

Count 1 is a generic count that appears in no patent or application. However, its breadth is similar to that of certain of Applicants' allowed independent claims, such as Applicants' Claim 443 reproduced much further below. As used in Count 1, the phrase "binding non-covalently" encompasses both specific hybridization and ligand-receptor interaction. The phrase "binding non-covalently to the analyte" encompasses not only direct binding to the analyte but also indirect binding via an intermediate entity(s) that in turn binds to the analyte. The term "binding" not followed by the term "non-covalently" encompasses both covalent and non-covalent binding. Finally, the term "immobilized" encompasses both direct and indirect and covalent and non-covalent binding to a solid or insoluble phase.

(3) Claims in Patents that Correspond to Count (37 C.F.R. § 1.607(a)(3))

The patent claims discussed below define species of the genus defined by Count 1. In other words, although the terminology and superficial features of these claims vary widely, the inventions defined by these claims are patentably indistinct from the generic invention. This is true even though the preambles of these claims differ from the preamble of Count 1 ("A hybridization or immuno assay for detecting an analyte") and are instead directed to methods for detecting analytes with hybridization assays, kits for carrying out such methods, compositions used for such methods, and so forth. Separate counts for these various types of claims are unnecessary because the "test for

claim correspondence is whether the count anticipates or renders obvious the claim.”³ The test is not whether the claim anticipates or renders obvious the count. In short, if Count 1 were prior art to these claims, it would anticipate or render them obvious.

Side-by-side comparisons of Count 1 with independent claims from the patents are set forth in the tables that follow. In addition to differing from Count 1 in terminology, these claims recite features in various orders that differ from the order in which Count 1 recites them. To help the reader quickly match features in these claims with the corresponding features in Count 1, the corresponding features are often flagged. Specifically, a select core term or phrase in Count 1 and a corresponding core term or phrase in a claim may be flagged with identical pairs of bold and superscripted letters that flank the corresponding terms or phrases. For example, in the first table below the term “analyte” in Count 1 corresponds to the term “target polynucleotide sequence” in Claim 1, so in Count 1 “analyte” is depicted as “^Banalyte^B” and in Claim 1 “target polynucleotide sequence” is depicted as “^Btarget polynucleotide sequence^B”. (The choice of letters is essentially arbitrary.) Similarly, “one or more bridge entities” in Count 1 and “primary probe” in Claim 1 are depicted as “^Done or more bridge entities^D” and “^Dprimary probe^D”. Please note that, when a feature is flagged in a table, it is flagged only once in that table. The letters do not flank repeated recitals of the same feature later in the Count or claim. Also, corresponding features and phrases are not flagged or discussed at all when their correspondence is self-evident or readily ascertainable in view of previous discussion.

In many of the tables, select features in the claims are also shaded (*e.g.*, shaded) to indicate that they are not explicitly recited in Count 1 but are either inherently present in Count 1 or obvious in view of it. For example, in the first table below Claim 1 recites “complex” and “single-stranded” polynucleotide sequences. These terms are not explicitly recited in Count 1. Nevertheless, as explained after the table, the features that these terms represent are either inherent in or obvious in view of Count 1. As with the flanking letters, features and phrases are not shaded when their inherency or obviousness is either self-evident or readily ascertainable in view of previous discussion.

³ Judge Michael Tierney, ‘Preliminary Tasks in Declaring the Interference,’ in tab H of handbook for IPO conference *PTO Appellate and Interference Practice in the New Millennium* (September 2002).

A. U.S. Patent No. 4,716,106

Claims 1-10 of the '106 Patent correspond substantially to Count 1 because they are directed to patentably indistinct species of Count 1. If Count 1 were prior art to Claims 1-10 of the '106 Patent, Count 1 would anticipate or render them obvious.

Compare, for example, paragraphs 4-6 of the Executive Summary above with this passage from the '106 Patent, which speaks to the gist and purpose of the claimed invention:

All these prior workers used a labelled single-stranded polynucleotide probe to hybridise with the target sequence. Each probe for each different assay has to be labelled separately. Labelling of the probe necessarily involves an additional preparative step, and one which may in some cases be difficult. The present invention seeks to avoid this problem by the use of a labelled secondary probe which does not have to be complementary to the target sequence and can therefore be used in assays for a variety of different targets.

'106 Patent, col. 2, lines 1-10 [emphasis added].

A side-by-side comparison of Count 1 and Claim 1 is set forth in Appendix B and in the table below.

Count 1	Claim 1 of US4716106
<p>A hybridization or immuno assay for detecting an ^Banalyte^B, comprising:</p> <p>(A) providing ^Done or more bridge entities^D, wherein each bridge entity comprises one or more first portions and one or more second portions, wherein each ^Gfirst portion is capable of binding non-covalently to the analyte^G, and wherein each ^Hsecond portion is capable of binding non-covalently to one or more signal probes and is substantially incapable of binding to the analyte^H;</p> <p>(B) providing said ^Kone or more signal probes^K, wherein each signal probe is ^Ocapable of binding non-covalently to at least one segment of the one or more second portions and is substantially incapable of binding to the analyte^O;</p> <p>(C) detecting the analyte by detecting one or more radioactive or nonradioactive signal moieties provided or afforded by the one or more signal probes; and</p> <p>(D) wherein optionally: (i) the analyte, bridge entities or signal probes are immobilized, or (ii) ^Xstep (B) is performed before step (A)^X.</p>	<p>A method of detecting a specific ^Btarget polynucleotide sequence in a sample^B, comprising the use of</p> <p>(a) a ^Klabelled polynucleotide secondary probe^K having a complex single-stranded polynucleotide sequence, and</p> <p>(b) a polynucleotide ^Dprimary probe^D having a single-stranded ^Gsequence complementary to the target sequence^G and a complex single-stranded ^Hsequence^H ^Ocomplementary to the complex sequence of the secondary probe^O, which method comprises the steps of</p> <p>(i) contacting the sample under hybridisation conditions with the primary probe,</p> <p>(ii) ^Xbefore, during or after said contact hybridising the labelled secondary probe to the primary probe^X, and</p> <p>(iii) observing the presence or absence of the label in association with the sample as indicating the presence or absence of the target sequence.</p>

As indicated by the flanking letters, the "target polynucleotide sequence" of Claim 1 of the '106 Patent corresponds to the "analyte" of Count 1. Similarly: "labelled polynucleotide secondary probe" in Claim 1 corresponds to "one or more signal probes" in Count 1; "primary probe"

corresponds to “one or more bridge entities”; “sequence complementary to the target sequence” corresponds to “first portion is capable of binding non-covalently to the analyte”; the third instance of “sequence” in step (b) of Claim 1 corresponds to “second portion is capable of binding non-covalently to one or more signal probes and is substantially incapable of binding to the analyte”; “complementary to...the secondary probe” corresponds to “capable of binding non-covalently to at least one segment of the one or more second portions...”; and “before, during or after said contact hybridising the labelled secondary probe to the primary probe” corresponds to “step (B) is performed before step (A).”

As indicated by the shading, Count 1 does not explicitly recite the “complex” and “single-stranded” polynucleotide sequences recited in Claim 1 of the ‘106 Patent. However, these features are inherent in or obvious in view of Count 1. The “single-stranded” feature is inherent in Count 1 because nucleic acid probes must be single-stranded or must become single-stranded to hybridize to other sequences. *See, e.g.*, ‘106 Patent, col. 3, lines 3-11. The “complex” feature is inherent in or obvious in view of Count 1 because “complex” means only that the polynucleotide is not a low-complexity sequence with uniform or highly repetitive residues. For example, naturally occurring DNA and RNA are usually complex. *See, e.g.*, ‘106 Patent, col. 2, lines 39-43. Since the use of both low-complexity and high-complexity sequences was well-known in this art, Count 1 encompasses the use of either.

Claims 2-10, which depend directly or indirectly from Claim 1, also correspond substantially to Count 1 because they fail to define separately patentable inventions in view of Count 1. Claim 2 recites that the sample is immobilized, which also was well-known in the art. Claim 3 recites that the sample is contacted by the primary probe before the secondary probe, which tracks Count 1 even more closely than Claim 1 does. Claim 4 recites that the primary and secondary probe are mixed before contact with the immobilized sample, which corresponds to optional step (D)(ii) of Count 1. Claims 5-7 and 9 recite that the primary or secondary probes are derived from a double-stranded vector, *i.e.*, they are cloned. Cloning probes (via double-stranded vectors) in conjunction with their use in assays was well-known in the art. Claim 8 is vague but appears to recite that the primary probe is single-stranded when it first contacts the sample, then partially double-stranded hybrids are formed between the primary probe and the sample, and then single-stranded secondary probes are added. These conventional steps do not render Claim 8 patentably distinct. Claim 10

recites that the primary probe is DNA and that the secondary probe is RNA. Forming RNA-DNA hybrids between probes was well-known in this art.

B. U.S. Patent No. 4,882,269

Claims 1-62 of the '269 Patent correspond substantially to Count 1 because they are directed to patentably indistinct species of Count 1. Compare, for example, paragraphs 3-6 of the Executive Summary above with these passages from the '269 Patent, which distinguish the prior art and speak to the gist and purpose of the claimed invention:

However, there are several disadvantages to these methods [of nucleic acid hybridization]. First, the production of probes requires the use of radioactive isotopes which have short half-lives necessitating a continuous production of fresh probes. Second, the labeling procedure requires the use of enzymes which are expensive and require reaction conditions which must be very carefully calibrated. Third, radioactive isotopes are biologically dangerous to use....

'269 Patent, col. 2, lines 23-31 [emphasis added].

Another problem encountered is that the alteration of the nucleotides interferes with hybridization of the probe to its target.

'269 Patent, col. 2, lines 47-49. See also '269 Patent, col. 7, lines 18-22 [emphasis added].

(i) Claims 1-24:

If Count 1 were prior art to Claims 1-24, Count 1 would anticipate or render them obvious.

A side-by-side comparison is set forth in the table below.

Count 1	Claim 1 of US4882269
A hybridization or immuno assay for detecting an ^B analyte ^B , comprising: (A) providing ^D one or more bridge entities ^D , wherein each bridge entity comprises one or more first portions and one or more second portions, wherein each ^G first portion is capable of binding non-covalently to the analyte ^G , and wherein each ^H second portion is capable of binding non-covalently to one or more signal probes and is substantially incapable of binding to the analyte ^H ; (B) providing said ^K one or more signal probes ^K , wherein each signal probe is ^O capable of binding non-covalently to at least one segment of the one or more second portions and is substantially incapable of binding to the analyte ^O ; (C) ^R detecting the analyte by detecting one or more radioactive or nonradioactive signal moieties provided or afforded by the one or more signal probes ^R ; and	A method for the detection of a ^B target nucleotide sequence ^B , comprising: (a) contacting the target nucleotide under conditions that permit hybridization with (i) a ^D primary probe ^D which comprises a polynucleotide ^G sequence that is complementary to the target nucleotide sequence ^G and a ^H polymeric tail that has binding sites that are incapable of binding to the target sequence ^H , and (ii) a ^K plurality of secondary probes comprising a family of signal-generating probes each member of which comprises a signal generating component ^K and a ^O polymer capable of binding to a different portion of the tail of the primary probe ^O ; and (b) ^R detecting the amplified signal generated by a reaction product formed in step (a), in which the polynucleotide sequence of the primary probe is hybridized to the target nucleotide and a plurality of

(D) wherein optionally: (i) the analyte, bridge entities or signal probes are immobilized, or (ii) step (B) is performed before step (A).	secondary probes are bound to different portions of the primary probe tail ^R .
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As indicated by their shading in the table above, the following phrases are not recited in Count 1: “polymer,” “polymeric tail,” “amplified,” “a different portion of the tail,” and “plurality of secondary probes are bound to different portions of the primary probe tail.” These features are inherent in or obvious in view of Count 1.

The Definitions section of the ‘269 Patent describes the “polymeric tail” and “polymer” of Claim 1 such that it is clear that they correspond, respectively, to the “second portion” and “signal probes” of Count 1.⁴ In the ‘269 Patent the “polymeric tail” and “polymer” are often mere nucleic acids. In fact, this embodiment is particularly preferred in the ‘269 Patent. *See* ‘269 Patent, col. 8, lines 38-46. Moreover, non-nucleic acid polymers were known in this art, which is why the ability to use them is not a point of invention for the ‘269 Patent and why its disclosure in this regard is cursory and general. *See, e.g.*, ‘269 Patent, col. 8, lines 28-37. Furthermore, Count 1’s embrace of immuno assays is inconsistent with exclusion of non-nucleic acid polymers.

With regard to “amplified” and “plurality of secondary probes are bound to [primary probe],” note that amplification of signals was known in this art. The ‘269 Patent itself states: “The detection of the primary hybridization event in hybridization assays previously described have

⁴ As stated in the ‘269 Patent:

The “primary probe” comprises a polynucleotide sequence which is complementary to the target sequence of interest attached to a “tail” that does not bind to the target sequence and is available for binding to other substances. The “tail” of the primary probe may comprise any of a number of polymers, including but not limited to single and double-stranded polynucleotides, and other natural or synthetic polymers such as cellulose, nylon, rayon, and the like. The primary probe may comprise linear or circular molecules.

The “secondary probes” comprise a family of signal-generating probes, each of which contains a segment capable of binding to a portion of the tail of the primary probe attached to a “signal-generating component”. The composition of the secondary probes is dependent upon the composition of the tail of the primary probe; for example, where the tail of the primary probe is a single-stranded polynucleotide, the secondary probes can comprise a family of polynucleotides each of which contains a single-stranded portion that hybridizes to a segment of the primary probe tail.

‘269 Patent, col. 5, lines 15-35.

generally not been amplified by secondary events.” ‘269 Patent, col. 4, lines 65-67 [emphasis added].

The ‘269 Patent attempts to distinguish the prior art as follows:

In these [prior art] systems, the magnitude of amplification is determined by the incorporation of reporter groups into the primary probe, and thus the signal to target ratio is severely restricted. The present invention discloses assays which provide for enormous amplification of the signal to target ratio by means of many secondary probe hybridization events directed to the primary probe....

‘269 Patent, col. 4, line 67 to col. 5, line 6 [emphasis added].

In other words, this type of amplification is achieved when more than one signal can attach to a “primary” detection probe. *See* ‘269 Patent, col. 22, lines 56-58. Yet, this type of amplification—many signals per detection probe—was also known in this art. Furthermore, Count 1 recites that each bridge entity comprises “one or more second portions” and that the “one or more signal probes” can bind to “at least a section of a second portion.” This quoted language from Count 1 provides at least three avenues by which a plurality of signal probes can bind to a detection probe so that the total number of bound signals well exceeds the number of bound detection probes, thereby amplifying the detection.

Regarding “a different portion of the tail” and “different portions of the primary probe tail,” Count 1 requires neither that each signal probe bind to identical second portions nor that each signal probe bind to identical sections of the second portions. Indeed, the fact that in Count 1 “one or more signal probes” can bind to “at least a section of a second portion” is consistent with multiple signal probes binding to different sections of a second portion.

The limitations added by Claims 2-24, which depend directly or indirectly from Claim 1, are obvious in view of Count 1. Indeed, in the Background section of the ‘269 Patent (col. 2-4) most of the added limitations are explicitly disclosed as being in the prior art.

(ii) Claims 25-48:

If Count 1 were prior art to Claims 25-48, Count 1 would anticipate or render them obvious. Claim 25 differs from Claim 1 mainly in that Claim 25 is directed to “A hybridization assay kit for the detection of a target nucleotide sequence...” rather than to “A method for the detection of a target nucleotide sequence...” Count 1, directed to “A hybridization or immuno assay for detecting an analyte,” would equally anticipate Claim 25 or render it obvious.

The limitations added by Claims 26-48, which depend directly or indirectly from Claim 25, are obvious in view of Count 1. Indeed, in the Background section of the ‘269 Patent (col. 2-4), most of the added limitations are explicitly disclosed as being in the prior art.

(iii) Claims 49-62:

If Count 1 were prior art to Claims 49-62, Count 1 would anticipate or render them obvious. A side-by-side comparison of Count 1 and Claim 49, the third independent claim of the '269 Patent, is set forth in Appendix B and in the table below.

Count 1	Claim 49 of US4882269 Patent
<p>A hybridization or immuno assay for detecting an ^Banalyte^B, comprising:</p> <p>(A) providing ^Done or more bridge entities^D, wherein each bridge entity comprises one or more first portions and one or more second portions, wherein each ^Gfirst portion is capable of binding non-covalently to the analyte^G, and wherein each ^Hsecond portion is capable of binding non-covalently to one or more signal probes and is substantially incapable of binding to the analyte^H;</p> <p>(B) providing said ^Kone or more signal probes^K, wherein each signal probe is ^Ocapable of binding non-covalently to at least one segment of the one or more second portions and is substantially incapable of binding to the analyte^O;</p> <p>(C) ^Rdetecting the analyte by detecting one or more radioactive or nonradioactive signal moieties provided or afforded by the one or more signal probes^R; and</p> <p>(D) wherein optionally: (i) the analyte, bridge entities or signal probes are immobilized, or (ii) step (B) is performed before step (A).</p>	<p>A hybridization assay kit for the detection of a ^Btarget nucleotide sequence^B, comprising:</p> <p>(a) a ^Dprimary probe cassette which comprises a cloning vector^D having</p> <p>(i) a ^Gmultiple cloning site into which a target nucleotide sequence can be inserted and cloned^G and</p> <p>(ii) ^Hnucleotide sequences which are capable of hybridizing to their complements which comprise a plurality of secondary probes^H; and</p> <p>(b) the ^Kplurality of secondary probes^K comprising a family of signal-generating probes each member of which comprises a signal-generating component and a nucleotide sequence ^Ocapable of hybridizing to a different portion of the portion of the primary probe described in (a)(ii)^O, which provides for the generation of an ^Ramplified signal when the plurality of secondary probes are hybridized to different portions of the portion of the primary probe^R described in (a)(ii).</p>

As indicated by the shading in the table above, the following two phrases are not recited in Count 1: “primary probe cassette which comprises a cloning vector” and “multiple cloning site into which a target nucleotide sequence can be inserted and cloned.” These features are inherent in or obvious in view of Count 1 and correspond to its bridge entities and first portions.

The bridge entities of Count 1 encompass, among other things, various types of polynucleotides including the cassette and vector type polynucleotides described in the '269 Patent. Cassette and vector type polynucleotides are the immediate precursors of detection probes and have long been used to produce detection probes for assays.⁵ Accordingly, the above-shaded phrases—

⁵ As stated in the '269 Patent:

(continued...)

“primary probe cassette which comprises a cloning vector” and “multiple cloning site into which a target nucleotide sequence can be inserted and cloned”—correspond to the bridge entities and first portions of Count 1.

The limitations added by Claims 50-62, which depend directly or indirectly from Claim 49, are obvious in view of Count 1. Indeed, in the Background section of the '269 Patent (col. 2-4), most of the added limitations are explicitly disclosed as being in the prior art.

C. U.S. Patent No. 5,424,188

Claims 1-19 of the '188 Patent correspond substantially to Count 1 because they are directed to patentably indistinct species of Count 1. If Count 1 were prior art to these claims, Count 1 would anticipate or render them obvious.

In practice, a polynucleotide primary probe may be constructed using the primary probe cassette by inserting and cloning the target sequence into the multiple cloning site and purifying the single stranded form of the resulting recombinant nucleotide vector.
'269 Patent, col. 5, lines 52-57.

The portion of the primary probe which is complementary to the target sequence...usually, but need not be, produced by cloning the target sequence into a recombinant vector such as a plasmid or virus which can be used to generate many copies of the sequence. Alternatively, the primary probes may be synthesized by chemical methods. These procedures are well known to one skilled in the art.
'269 Patent, col. 8, lines 17-26.

When both primary probe including its tail comprise polynucleotides, the entire probe can be relatively easily generated through recombinant DNA techniques. Accordingly, the primary probe may be cloned using a recombinant vector such as plasmid or viral DNA. In fact, the primary probe may comprise the entire length of a recombinant vector molecule which contains the target sequence.

Vector systems which provide a particular advantage for the cloning and production of single stranded primary probes comprise vectors derived from the filamentous bacteriophages such as M13 and f1. These phage vectors are capable of producing large quantities of easily purified single stranded DNA molecules in complementary orientations.
'269 Patent, col. 8, lines 43-57.

Radioactively labeled or biotinylated *Escherichia coli* single strand DNA binding protein (SSB) crosslinked to filamentous phage M13 ssDNA containing a nucleic acid sequence complementary to the target gene has recently been used as a probe in a hybridization assay system (Synaven et al., 1985, Nucl. Acids. Res. 13, 2789-2802).
'269 Patent, col. 2, lines 57-63 (the Background section).

Note that on October 14, 1994, the applicants for the '188 Patent terminally disclaimed it over the '269 Patent. Thus, they acquiesced to the proposition that the claims of the '269 Patent are patentably indistinct from those of the '188 Patent, which strongly suggests that the claims from each will correspond to the same count.

A side-by-side comparison between Count 1 and Claim 1 is set forth in Appendix B and in the table below. Claim 1 is so similar to the claims of the '269 Patent discussed above that no flags, shading, or further discussion is included below.

Count 1	Claim 1 of US5424188
<p>A hybridization or immuno assay for detecting an analyte, comprising:</p> <p>(A) providing one or more bridge entities, wherein each bridge entity comprises one or more first portions and one or more second portions, wherein each first portion is capable of binding non-covalently to the analyte, and wherein each second portion is capable of binding non-covalently to one or more signal probes and is substantially incapable of binding to the analyte;</p> <p>(B) providing said one or more signal probes, wherein each signal probe is capable of binding non-covalently to at least one segment of the one or more second portions and is substantially incapable of binding to the analyte;</p> <p>(C) detecting the analyte by detecting one or more radioactive or nonradioactive signal moieties provided or afforded by the one or more signal probes; and</p> <p>(D) wherein optionally: (i) the analyte, bridge entities or signal probes are immobilized, or (ii) step (B) is performed before step (A).</p>	<p>A hybridization assay kit for the detection of a target nucleotide sequence in a sample which target is hybridized to a primary probe, which primary probe has</p> <p>(1) a polynucleotide sequence complementary to the target nucleotide sequence and</p> <p>(2) a polymeric tail with a plurality of binding sites, each site incapable of binding to the target sequence and capable of binding a member of a family of secondary probes, which kit comprises:</p> <p>a plurality of secondary probes comprising a family of signal-generating probes, each member of the family having at least (1) a signal-generating component and</p> <p>(2) a polymer capable of binding to a distinct binding site of the tail of the primary probe which site is not bound by other members of the family;</p> <p>which kit provides for the generation of an amplified signal when the plurality of secondary probes are bound to distinct binding sites of the tail of the primary probe.</p>

The limitations added by Claims 2-19, which depend directly or indirectly from Claim 1, are obvious in view of Count 1. Indeed, in the Background section of the '188 Patent (col. 2-4) most of the added limitations are explicitly disclosed as being in the prior art.

D. US Patent No. 5,124,246

Claims 39-41, 43-56 and 58-59 of the '246 Patent correspond substantially to Count 1 because they are directed to patentably indistinct species of Count 1.

Consider the following passages from the '246 Patent, which speak to the gist and purpose of the claimed invention. But bear in mind that the '246 Patent not only uses different terminology, it uses terminology inconsistently. In some '246 patent claims, the "multimer" (or multi-part

polynucleotide) corresponds to the signal probe of Count 1, and the “amplifier probe” corresponds to the bridge entity of Count 1. In other ‘246 patent claims, the multimer corresponds to the bridge entity and the amplifier probe is not recited.

A primary object of the present invention is to provide an amplifier for use in nucleic acid hybridizations that provides a high reproducible gain in signal...and that is capable of combining specifically with a “universal” signal moiety and an analyte at low concentrations to form a stable complex.

‘246 Patent, col. 2, lines 6-13 [emphasis added].

By using an amplifier probe, the multimer may be designed to be a “universal” reagent and different multimers need not be made for each analyte.

‘246 Patent, col. 14, lines 39-41 [emphasis added].

Again, the ‘246 Patent uses terminology that differs from both Count 1 and the foregoing patents. Most of the differences reflect the fact that the ‘246 patent claims suffer from “over claiming,” *i.e.*, they are verbose and peripheral and they explicitly recite characteristics of features that are subsumed in the common names for those features.⁶ Accordingly, to adequately compare Count 1 to the ‘246 Patent claims, one must distill the underlying structure and steps defined by the claims and not be misled by their appearance.

(i) Claims 39-41 and 43-52:

Despite its elaborate wording, independent Claim 39 boils down to the following: a synthetic linear polynucleotide having three or more segments, wherein one segment hybridizes to a first sequence of interest and the other segments hybridize to a second sequence of interest. Claim 39 corresponds substantially to Count 1, despite that Claim 39 is directed to a multimer used in an assay rather than to the assay itself. Specifically, the multimer of Claim 39 corresponds to the bridge entity of Count 1, which would anticipate Claim 39 or render it obvious. The fact that Count 1 is directed to an assay that uses the bridge entity—and not to a bridge entity that is used in the assay—does not change this.⁷ A side-by-side comparison is set forth in Appendix B and in the table below.

⁶ For example, if the drafters of the ‘246 Patent needed to recite a basketball, they might have recited something like “a spherical article comprising durable and elastic exterior walls that encase a pressurized gas, wherein the radius of the article...”

⁷ Again, the “test for claim correspondence is whether the count anticipates or renders obvious the claim.” Judge Tierney, *supra*. The test is not whether the claim anticipates or renders obvious the count. Although a count directed to a multimer may or may not render obvious a claim to an assay that uses the multimer, a count to an assay that uses the multimer should render obvious a claim to the multimer.

Count 1	Claim 39 of US5124246
<p>A^A hybridization or immuno assay^A for detecting an analyte, comprising:</p> <p>(A) providing ^Done or more bridge entities^D, wherein each bridge entity comprises one or more first portions and one or more second portions, wherein each ^Gfirst portion is capable of binding non-covalently to the analyte^G, and wherein each ^Hsecond portion is capable of binding non-covalently to one or more signal probes and is substantially incapable of binding to the analyte^H;</p> <p>(B) providing said one or more signal probes, wherein each signal probe is capable of binding non-covalently to at least one segment of the one or more second portions and is substantially incapable of binding to the analyte;</p> <p>(C) ^Rdetecting the analyte by detecting one or more radioactive or nonradioactive signal moieties provided or afforded by the one or more signal probes^R; and</p> <p>(D) wherein optionally: (i) the analyte, bridge entities or signal probes are immobilized, or (ii) step (B) is performed before step (A).</p>	<p>A^D synthetic linear nonhomopolymeric nucleic acid multimer^D useful as a means for ^Ramplifying a detectable signal^R in an ^Aassay involving nucleic acid hybridization^A consisting essentially of:</p> <p>(a) at least one ^Gfirst single-stranded oligonucleotide unit that is capable of hybridizing specifically to a first single-stranded nucleic acid sequence of interest^G; and</p> <p>(b) a ^Hmultiplicity of second single-stranded oligonucleotide units all of which are capable of hybridizing specifically to a second single-stranded nucleic acid sequence of interest^H, wherein the first single-stranded oligonucleotide unit is bonded directly or indirectly to the multiplicity of second single-stranded oligonucleotide units only via covalent bonds.</p>

The above-shaded features are inherent in or obvious in view of Count 1. The “nucleic acid multimer” (recited in the phrase “synthetic linear nonhomopolymeric nucleic acid multimer”) is simply a multi-segment polynucleotide. “Synthetic” means it is man-made. “Linear” means it is straight, *i.e.*, not branched or circular. “Nonhomopolymeric” is not explained in and does not appear elsewhere in the ‘246 Patent. However, during prosecution the applicants for the ‘246 Patent stated that: “The term ‘nonhomopolymeric’ ... is believed to be inherent in the [applicants’] use of the terms ‘multimer’ and ‘oligonucleotide unit’.”⁸ Further, at least one biotechnology dictionary defines the base word “homopolymer” as follows: “In general meaning, any polymeric molecule containing a single type of monomer. In molecular biology, the term refers to a short nucleic acid segment that consists of a single type of nucleotide, for example, oligo dT.”⁹ For the base word

⁸ File History of ‘246 Patent, Amendment of March 1, 1990 (p.9,11).

⁹ Mark L. Steinberg, PH.D. and Sharon D. Cosloy, PH.D, The Facts on File Dictionary of Biotechnology and Genetic Engineering, p. 106 (2001).

“homopolymer,” this definition appears to be the one that the ‘246 applicants had in mind.¹⁰ In any event, Count 1 encompasses various types of polymers including both homopolymers and nonhomopolymers.

The following phrases are also shaded in the table above: “first single-stranded nucleic acid sequence of interest” and “second single-stranded nucleic acid sequence of interest.” As indicated by the dependent claims (such as Claim 48), the first sequence of interest is simply an analyte or a nucleic acid that can directly or indirectly bind to an analyte. The second sequence of interest, as indicated by the dependent claims (such as Claim 51), is simply a signal probe or a nucleic acid that can directly or indirectly bind to a signal probe.

The shaded phrase “only via covalent bonds” means that the segments of the multimer are not hybridized to each other. Rather, they have been ligated or joined together with cross-linking agents, using conventional techniques. *See, e.g.*, ‘246 Patent, col. 9, lines 31-53 and col. 10, lines 28-36. Note that the phrase “binding non-covalently” in Count 1 refers only to bonds between the bridge entity and the analyte, or to bonds between the bridge entity and the signal probes. It does not refer to bonds between the first and second portion(s) of the bridge entity, which are usually covalent in the invention defined by Count 1. In sum, the reference in Claim 39 to “only covalent bonds” between the first oligonucleotide unit and the second oligonucleotide units corresponds to the bonds in Count 1 between the first portion and second portion(s) of the bridge entity.

The limitations added by Claims 40-41 and 43-52, which depend directly from Claim 39, are obvious in view of Count 1.

(ii) Claims 53-56 and 58-59:

Claims 53-56 and 58-59 also correspond substantially to Count 1. Claim 53 depends from Claim 51 which depends from Claim 39. In the ‘246 Patent, Claim 53 starts as: “A nucleic acid hybridization assay wherein: (a) the multimer of claim 51 is...” In turn, Claim 51 reads: “The nucleic acid multimer of claim 39 wherein the second single-stranded nucleotide sequence of interest is a sequence of a single-stranded labeled oligonucleotide.” The edited version of Claim 53 below (and in Appendix B) incorporates the relevant text of Claims 39 and 51.

¹⁰ *See, e.g.*, File History of ‘246 Patent, Amendment of March 1, 1990 (p.11) and Amendment of February 19, 1991 (p.5-6).

Count 1	Claim 53 of US5124246
<p>A hybridization or immuno assay for detecting an analyte, comprising:</p> <p>(A) providing one or more bridge entities, wherein each bridge entity comprises one or more first portions and one or more second portions, wherein each first portion is capable of binding non-covalently to the analyte, and wherein each second portion is capable of binding non-covalently to one or more signal probes and is substantially incapable of binding to the analyte;</p> <p>(B) providing said ^Kone or more signal probes^K, wherein each signal probe is capable of binding non-covalently to at least one segment of the one or more second portions and is substantially incapable of binding to the analyte;</p> <p>(C) detecting the analyte by detecting one or more radioactive or nonradioactive signal moieties provided or afforded by the one or more signal probes; and</p> <p>(D) wherein optionally: (i) ^Tthe analyte, bridge entities or signal probes are immobilized^T, or (ii) step (B) is performed before step (A).</p>	<p>A nucleic acid hybridization assay wherein:</p> <p>I. provided is a synthetic linear nonhomopolymeric nucleic acid multimer useful as a means for amplifying a detectable signal in an assay involving nucleic acid hybridization consisting essentially of:</p> <p>(a) at least one first single-stranded oligonucleotide unit that is capable of hybridizing specifically to a first single-stranded nucleic acid sequence of interest; and</p> <p>(b) a multiplicity of second single-stranded oligonucleotide units all of which are capable of hybridizing specifically to a second single-stranded nucleic acid sequence of interest that comprises a ^Ksingle-stranded labeled oligonucleotide^K, wherein the first single-stranded oligonucleotide unit is bonded directly or indirectly to the multiplicity of second single-stranded oligonucleotide units only via covalent bonds;</p> <p>II. the multimer is hybridized via the first oligonucleotide unit to single-stranded analyte nucleic acid ^Tbound to a solid phase^T or to a single-stranded oligonucleotide bound to the analyte;</p> <p>III. unbound multimer is removed;</p> <p>IV. single-stranded labeled oligonucleotide is hybridized to the multimer via the second oligonucleotide units;</p> <p>V. unbound labeled oligonucleotide is removed; and</p> <p>VI. the presence of label bound to the multimer is detected.</p>

The shaded phrase “or to a single-stranded oligonucleotide bound to the analyte” is obvious in view of Count 1. As explained in Section (2) of this Request (Presentation of Proposed Count), the phrase in Count 1 about the bridge entity “binding non-covalently to the analyte” includes not only direct non-covalent binding to the analyte but also non-covalent binding to an intermediate sequence or other entity that binds to the analyte.

The shaded phrases “unbound multimer is removed” and “unbound labeled oligonucleotide is removed” are also obvious in view of Count 1. These phrases denote conventional washing steps that were well-known in this art.

Claims 54-56, which depend from Claim 53, and Claims 58-59, which depend from Claim 39, recite obvious variants. For example, Claims 58-59 mirror Claim 53 except that in Claims 58-59

the multimer merely binds to a ligand that in turn binds to the analyte. This would be obvious even if Count 1 did not encompass immuno assays, which it expressly does.

(4) Claims of Application that Correspond to Count (37 C.F.R. § 1.607(a)(4))

Claims 283-362, 364-380, 382-398, 400-404, 406-439, and 441-505, all of which have been allowed, correspond substantially to Count 1.¹¹ Representative independent claims include: composition Claim 283; article of manufacture Claim 360; process Claims 443 and 460; and kit Claim 411. Side-by-side comparisons between Count 1 and these representative claims are set forth in the tables below and in Appendix C.

Count 1	Claim 283 of Pergolizzi Application
<p>A hybridization or immuno assay for detecting an analyte, comprising:</p> <p>(A) providing ^Done or more bridge entities^D, wherein each bridge entity comprises one or more first portions and one or more second portions, wherein each ^Gfirst portion is capable of binding non-covalently to the analyte^G, and wherein each ^Hsecond portion is capable of binding non-covalently to one or more signal probes and is substantially incapable of binding to the analyte^H;</p> <p>(B) providing said ^Kone or more signal probes^K, wherein each signal probe is ^Ocapable of binding non-covalently to at least one segment of the one or more second portions and is substantially incapable of binding to the analyte^O;</p> <p>(C) ^Rdetecting the analyte by detecting one or more radioactive or nonradioactive signal moieties provided or afforded by the one or more signal probes^R; and</p> <p>(D) wherein optionally: (i) the analyte, bridge entities or signal probes are immobilized, or (ii) step (B) is performed before step (A).</p>	<p>A composition of matter comprising:</p> <p>a ^Dfirst part which comprises a molecular bridging entity^D comprising a ^Gfirst portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte^G, and a ^Hsecond portion comprising one or more nucleic acid sequences or segments^H; and</p> <p>a second part which comprises ^Kone or more non-radioactive signalling entities^K ^Osubstantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion^O, and ^Rone or more signal generating portions capable of providing a detectable signal^R.</p>

Essentially, Claim 283 defines the reaction mixture of the bridge entity and signal probes. Although Claim 283 is directed to a “composition of matter” used in an assay rather than to the

¹¹ Missing claims 363, 381, 399, 405 and 440 were previously canceled.

assay itself, it substantially corresponds to Count 1. Were the assay of Count 1 prior art to the composition of Claim 283, Count 1 would render it obvious.

The phrase "molecularly recognizable" means only that the first portion binds or hybridizes with specificity to the analyte, that is, it will not bind or hybridize to just anything.

Count 1	Claim 360 of Pergolizzi Application
<p>A hybridization or immuno assay for detecting an analyte, comprising:</p> <p>(A) providing one or more bridge entities, wherein each bridge entity comprises one or more first portions and one or more second portions, wherein each first portion is capable of binding non-covalently to the analyte, and wherein each second portion is capable of binding non-covalently to one or more signal probes and is substantially incapable of binding to the analyte;</p> <p>(B) providing said one or more signal probes, wherein each signal probe is capable of binding non-covalently to at least one segment of the one or more second portions and is substantially incapable of binding to the analyte;</p> <p>(C) detecting the analyte by detecting one or more radioactive or nonradioactive signal moieties provided or afforded by the one or more signal probes; and</p> <p>(D) wherein optionally: (i) the analyte, bridge entities or signal probes are immobilized, or (ii) step (B) is performed before step (A).</p>	<p>An article of manufacture comprising:</p> <p>a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and</p> <p>more than one non-radioactive signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity second portion nucleic acid sequences or segments, and one or more signal generating portions, each capable of providing a detectable signal.</p>

Although Claim 360 is directed to an "article of manufacture" used in an assay rather than to the assay itself, it substantially corresponds to Count 1. Were the assay of Count 1 prior art to the article of Claim 360, Count 1 would render it obvious.

Count 1	Claim 411 of Pergolizzi Application
<p>A hybridization or immuno assay for detecting an analyte, comprising:</p> <p>(A) providing one or more bridge entities, wherein each bridge entity comprises one or more first portions and one or more second portions, wherein each first portion is capable of binding non-covalently to the analyte, and wherein each second portion is capable of binding non-covalently to one or more signal probes and is substantially incapable</p>	<p>A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof:</p> <p>(i) a container carrying a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with said molecularly recognizable portion on said analyte, and a second portion comprising one, or more nucleic acid sequences or segments; and</p>

<p>of binding to the analyte;</p> <p>(B) providing said one or more signal probes, wherein each signal probe is capable of binding non-covalently to at least one segment of the one or more second portions and is substantially incapable of binding to the analyte;</p> <p>(C) detecting the analyte by detecting one or more radioactive or nonradioactive signal moieties provided or afforded by the one or more signal probes; and</p> <p>(D) wherein optionally: (i) the analyte, bridge entities or signal probes are immobilized, or (ii) step (B) is performed before step (A).</p>	<p>(ii) a container carrying more than one non-radioactive signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity second portion nucleic acid sequence or segment, and one or more signal generating portions, each such portion being capable of providing a detectable signal.</p>
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Although Claim 411 is directed to a "kit" for an assay rather than to the assay itself, it substantially corresponds to Count 1. Were the assay of Count 1 prior art to the kit of Claim 411, Count 1 would render it obvious.

The "container" recited in Claim 411 is inherent in or obvious in view of the assay of Count 1.

Count 1	Claim 443 of Pergolizzi Application
<p>A hybridization or immuno assay for detecting an analyte, comprising:</p> <p>(A) providing one or more bridge entities, wherein each bridge entity comprises one or more first portions and one or more second portions, wherein each first portion is capable of binding non-covalently to the analyte, and wherein each second portion is capable of binding non-covalently to one or more signal probes and is substantially incapable of binding to the analyte;</p> <p>(B) providing said one or more signal probes, wherein each signal probe is capable of binding non-covalently to at least one segment of the one or more second portions and is substantially incapable of binding to the analyte;</p> <p>(C) detecting the analyte by detecting one or more radioactive or nonradioactive signal moieties provided or afforded by the one or more signal probes; and</p> <p>(D) wherein optionally: (i) the analyte, bridge entities or signal probes are immobilized, or (ii) step (B) is performed before step (A).</p>	<p>A process for detecting an analyte having one or more molecularly recognizable portions thereon, comprising:</p> <p>providing a composition of matter comprising:</p> <p>a first part which comprises a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and</p> <p>a second part which comprises one or more signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more signal generating portions capable of providing a detectable signal;</p> <p>forming a complex comprising said composition and said analyte; and</p> <p>detecting said analyte by a signal provided by</p>

	said signal generating portion or portions present in said complex.
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Although Claim 443 is directed to a “process for detecting” an analyte in an assay rather than to the assay itself, it substantially corresponds to Count 1. Were the assay of Count 1 prior art to the process of Claim 443, Count 1 would render it obvious.

The phrase “forming a complex” refers to the complex that is inherently formed in the assay of Count 1.

Count 1	Claim 460 of Pergolizzi Application
<p>A hybridization or immuno assay for detecting an analyte, comprising:</p> <p>(A) providing one or more bridge entities, wherein each bridge entity comprises one or more first portions and one or more second portions, wherein each first portion is capable of binding non-covalently to the analyte, and wherein each second portion is capable of binding non-covalently to one or more signal probes and is substantially incapable of binding to the analyte;</p> <p>(B) providing said one or more signal probes, wherein each signal probe is capable of binding non-covalently to at least one segment of the one or more second portions and is substantially incapable of binding to the analyte;</p> <p>(C) detecting the analyte by detecting one or more radioactive or nonradioactive signal moieties provided or afforded by the one or more signal probes; and</p> <p>(D) wherein optionally: (i) the ^Tanalyte, bridge entities or signal probes are immobilized^T, or (ii) step (B) is performed before step (A).</p>	<p>A process for detecting an analyte having one or more molecularly recognizable portions thereon, comprising:</p> <p>^Tfixing or immobilizing said analyte or a sample containing said analyte to a solid support^T;</p> <p>providing a composition comprising a complex which comprises:</p> <p>a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and</p> <p>one or more signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more chemically modified or artificially altered polynucleotides capable of providing a detectable signal;</p> <p>forming a complex comprising said composition and said analyte; and</p> <p>detecting said analyte by a signal provided by means of said signal generating portion or portions present in said complex.</p>

Claim 460 substantially corresponds to Count 1. Were the assay of Count 1 prior art to the process of Claim 460, Count 1 would render it obvious. As suggested by the Executive Summary,

the feature recited in Claim 460 as “chemically modified or artificially altered polynucleotides capable of providing a detectable signal” is inherent in or obvious in view of Count 1.

(5) Identification of Support in Application for New Claims (37 C.F.R. § 1.607(a)(5))

Under 37 C.F.R. § 1.607(a)(5), Applicants must apply the terms of an application claim to the disclosure of the application when the claim was (i) designated as corresponding to the count, and (ii) not previously in the application. In the present case, all of the claims designated as corresponding to the Count were previously in the Application.

(6) How Requirements of 35 U.S.C. § 135(b) Were Met (37 C.F.R. § 1.607(a)(6))

Section 135(b) requires that there was once pending, on or prior to the one-year anniversary of the issuance of a patent in question, at least one application claim directed to the “same or substantially the same subject matter” as at least one claim in the patent. *See also* 37 C.F.R. § 1.607(a)(6) and 37 C.F.R. § 1.601(j). The application claim need not claim an identical invention. *See* Case v. CPC Int'l Inc., 730 F.2d 745, 749, 221 USPQ 196, 200 (Fed. Cir 1984), *cert. denied*, 469 US 872, 224 USPQ 736 (1984) (regarding interference-in-fact). Indeed, the claims need not overlap. *See* Aelony v. Arni, 547 F.2d 566, 570, 192 USPQ 486, 489-90 (CCPA 1977) (regarding interference-in-fact). But the application claim should explicitly or inherently contain or result in the material limitations recited in the patent claim. *See, e.g.*, In re Berger, 61 U.S.P.Q.2d 1523, 1527-1528 (CAFC 2002); Berman v. Housey, 63 USPQ2d 1023, 1030-31 (Fed. Cir. 2002); Corbett v. Chisholm, 568 F.2d 759, 765-66, 196 U.S.P.Q. 337, 343 (CCPA 1977); In re Schutte, 244 F.2d 323, 326, 113 U.S.P.Q. 537, 540 (CCPA 1957). *See also* Parks v. Fine, 773 F.2d 1577, 1579, 227 U.S.P.Q. 432, 434 (CAFC 1985).

The '106 Patent issued December 29, 1987; the '269 Patent issued November 21, 1989; the '246 Patent issued June 23, 1992; and the '188 Patent issued June 13, 1995. Hence, the relevant dates under Section 135(b), *i.e.*, the one-year anniversary dates, are December 29, 1988; November 21, 1990; June 23, 1993; and June 13, 1996.

Attached Appendix D sets forth a non-exhaustive list of Pergolizzi claims that were pending before December 29, 1988; November 21, 1990; June 23, 1993; and June 13, 1996. In some cases, these Pergolizzi claims do not explicitly recite each and every last one of the phrases recited in the

issued patent claims that correspond to Count 1. However, those phrases either represent immaterial features or the Pergolizzi sample claims inherently contain or result in the features for reasons identical or similar to the reasons set forth throughout Section (3) of this Request. Finally, although many of the Pergolizzi claims in Appendix D were later amended or replaced, the current Pergolizzi claims continue to be directed to substantially the same subject matter as Count 1.

CONCLUSION

Applicants respectfully request that an interference employing Proposed Count 1 be declared between:

(I) Pergolizzi Application Claims 283-362, 364-380, 382-398, 400-404, 406-439, and 441-505; and

(II)(A) Claims 1-10 of U.S. Patent No. 4,716,106,

(II)(B) Claims 1-62 of U.S. Patent No. 4,882,269,

(II)(C) Claims 1-19 of U.S. Patent No. 5,424,188, and

(II)(D) Claims 39-41, 43-56 and 58-59 of U.S. Patent No. 5,124,246.

If the Examiner has any questions about this Request or about the above-identified Application, the Examiner is invited to contact the undersigned attorneys.

Respectfully Submitted

HUNTON & WILLIAMS

Dated: Dec. 20, 2002

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Pergolizzi et al.

Serial No.: 08/479,995

Filed: June 7, 1995

Page 2 [Communication To Introduce Request For An Interference
Pursuant To 37 C.F.R. §1.607 -- December 20, 2002]

REMARKS

This Communication follows a brief telephone conversation on December 19, 2002 between Examiner Ardin H. Marschel, Ph.D., Group Art Unit 1631, and Applicants' undersigned attorney. During that conversation, Applicants' attorney indicated that the effect of the three PTO Communications issued in March of 2000, 2001 and 2002 had been to suspend (or re-suspend) *ex parte* prosecution due to a potential interference. Since nearly three years have elapsed since the March 14, 2000 PTO Communication, Applicants respectfully request that the PTO promptly declare the interference.¹ To help avoid further delay, Applicants are submitting herewith attached as Exhibit 1 a Request For An Interference Under 37 C.F.R. §1.607.

Applicants' attorney understands that the delay in declaring the interference may be the result of lost or misplaced file wrappers in the PTO. Applicants wish to point out that complete copies of the file wrappers for the patents believed to be in question were obtained from a commercial file wrapper service (Patent Providers, Inc.) apparently without any delay or difficulties. Presumably, this commercial service obtained those file wrappers from the PTO. In any event, Applicants are more than happy to provide the PTO with paper or CD-ROM copies of the file wrappers that are in the possession of the Assignee. These file wrappers also include the present application and its predecessor applications.

¹ It is noted that in the March 19, 2002 PTO Communication, *ex parte* prosecution was suspended for a period of six (6) months, meaning that the suspension ended on September 19, 2002.

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Serial No.: 08/479,995

Filed: June 7, 1995

Page 3 [Communication To Introduce Request For An Interference

Pursuant To 37 C.F.R. §1.607 -- December 20, 2002]

Furthermore, should any file wrappers continue to be unavailable, the parties can avail themselves of the provisions of 37 C.F.R. §1.612 (Access to applications). Subsection (d) of §1.612 states:

The parties at any time may agree to exchange copies in the files of any application identified in the notice declaring the interference.

Favorable action on this application and the attached §1.607 Request is respectfully requested.

No fee is believed due in connection with the filing of this Communication, the purpose of which is to introduce Applicants' Request For An Interference Under 37 C.F.R. §1.607. In the event that any other fee or fees are due, however, The Patent and Trademark Office is hereby authorized to charge the amount of any such fee(s) to Deposit Account No. 05-1135, or to credit any overpayment thereto.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney request that he be contacted at the number provided below.

Respectfully submitted,



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